



Study of Hyperlipidimia and Gene Polymorphism Responsible for Fat Metabolism in Cardiovascular Diseases

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Resume: Today, overweight and obesity remain one of the most important global health problems in the world. Overweight and obesity are the cause of not only the appearance of all people, but also a number of diseases, including atherosclerosis and cardiovascular diseases, hypertension, ischemic and hemorrhagic stroke, as well as all other serious problems of internal organs. Development of methods for correcting hyperlipidemia based on gene polymorphism, responsible for the metabolism of fats in diseases of the cardiovascular system. Thus, in patients with cardiovascular diseases, hyperthyroidism was corrected for 7 out of three genes: cholesterol, HDL and LDL levels were higher in the original group and lower in the control group.

Key words: Hyperlipidimia, Polymorphism, Metabolism.

Relevance: Today, overweight and obesity remain one of the most important global health problems in the world. Overweight and obesity are not only the appearance of all people, but also cause a number of diseases, such as atherosclerosis and cardiovascular diseases, hypertension, ischemic and hemorrhagic stroke and other serious problems of all internal organs. In addition, excess body weight negatively affects the endocrine system and increases the risk factor for the development of diabetes, while obesity can lead to male or female infertility [22,23,25]. Non-compliance with the diet and some genetic characteristics of the patient can be the cause of the development of metabolic syndrome [1, 11, 15, and 19].

Today, overweight and obesity are among the top five risk factors for death. According to statistics, at least 3.4 million adults die each year due to being overweight or obese [24,27,29]. In addition, overweight has been found to be associated with 44% of diabetes, 23% of cardiovascular disease, and 7% - 41% of cancer [2,10,20,21].

The prevalence of obesity among children and adolescents is increasing significantly in developed countries and is 23.8% among boys and 22.6% among girls. About 25% of people of working age in Russia are obese and 30% are overweight. Projections in this situation suggest that by 2030, more than 2 billion people will be overweight and 1 billion will be obese [3,9,15,18].

Thus, compared to the information in the literature, the essence of genes, their dependence on hyperlipidemia in people with excess body weight and obesity has not been fully studied, and a

number of problems regarding the study of these genes are waiting for their solution. Among these, one of the most important global problems is the study of genes responsible for overweight and obesity, depending on hyperlipidemia. In the medical practice of Uzbekistan, methods of determining and correcting the dependence of genes on hyperlipidemia in overweight and obesity have not been developed and are not used in practice [26,28,30]. In order to eliminate the above-mentioned shortcomings, it is necessary to continue scientific research, as it is of great importance to medical practice to determine the dependence of genes on hyperlipidemia in overweight and obesity and to prevent the diseases that cause it.

Purpose: To develop ways to correct hyperlipidemia based on polymorphism of genes responsible for fat metabolism in diseases of the cardiovascular system.

Materials and methods: research was conducted on 54 patients with excess body weight treated in different departments of the multidisciplinary medical center of Bukhara region in 2019-2020. Of the 54 patients studied, 30 were in the control group, 24 were in the main cardiovascular group. Distributed to the system.

Results:

During the study, three genes – ADRB2 (rs1042713) A>G; ADRB3 (rs4994) Trp64Arg and PPARG2 (rs1801282)_C34G were studied, as well as seven related genotypes – A/A; A/G; Trp/Trp; Trp/Arg; C/G; C/C; The G/G encounter rate was also analyzed (Table 1).

Table 1 Age and gender of patients diagnosed with diseases of the cardiovascular system

Genes	Genotypes	Age		Gender			
				Male		Female	
		MG	CG	MG	CG	MG	CG
ADRB2(rs1042713) A>G	A/A	53,0	27,5	16/50,0	4/50,0	12/44,4	4/57,1
	A/G	52,3	25,6	16/50,0	4/50,0	15/55,6	3/42,9
ADRB3(rs4994) Trp64Arg	Trp/Trp	52,1	26,5	28/87,5	6/75,0	27/100,0	7/100,0
	Trp/Arg	59,0	27,0	4/12,5	2/25,0	0/0	0/0
PPARG2(rs1801282)_C34G	C/G	53,3	23,5	20/62,5	3/37,5	4/14,8	1/14,2
	C/C	51,5	28,7	12/37,5	4/50,0	19/70,4	5/71,4
	G/G	57,0	23,0	0/0	1/12,5	4/14,8	1/14,2
Summary		54,03	26,0	32/54	8/53	27/46	7/47

Note: the figures are absolute; the denominator is relative (%); MG – main group; CG – control group.

The obtained results showed that the level of meeting of genes and genotypes was mainly observed between 51.5 and 59.0 years (average age 54.03 years) in the main group: between 23.0 and 28.7 years (average age 26.0 years) in the control group. Observed. While the age gradations for the mentioned genes were equally distributed, they were somewhat different for the genotypes. S/S (51.5 years), Trp/Trp (52.1 years) and A/G (52.3 years) genotypes were more common in relatively young patients, while G/G (57.0 years) and Trp/Arg (59.0 years) genotypes were detected in slightly older patients. A significant difference in age between patients in the main and control groups was noted.

When analyzing the status depending on sex, the level of gene and genotypes was close to each other in men belonging to the main (n=32) and control (n=8) groups. ADRB2(rs1042713) A>G gene expression level was the same in both groups, similar values were observed in ADRB3(rs4994) Trp64Arg and PPARG2(rs1801282)_C34G genes.

However, some difference between the groups was found in the level of genotypes in men - Trp/Trp, C/G genotypes were more frequent in the main group compared to the control group, while Trp/Arg,

C/C and G/G genotypes were less frequent, respectively. It should be noted that among all 7 genotypes in the men of the main group, Trp/Trp (28 out of 32 cases, 87.5%), C/G (20 out of 32 cases, 62.5%) genotypes occurred more than 50% of the result. In the control group, a higher incidence rate was observed only in the Trp/Trp genotype (6 cases out of 8, 75.0%).

The results in women are slightly different from those of men. In the main group, Trp/Trp (27 out of 27 cases, 100.0%), C/C (19 out of 27 cases, 70.4%), A/G (15 out of 27 cases, 55.6%) genotypes while the incidence rate was high, different results were obtained in control group women - Trp/Trp (4 out of 7 cases, 57.1%) genotypes were more frequent in them. Trp/Trp in men in the main group; Trp/Arg; C/G genotypes were more common, while Trp/Trp, C/C, A/G genotypes were more common in women in the main group. In men of the control group, the Trp/Trp genotype exceeded the threshold of 50%, and in addition to the Trp/Trp genotype, the women in this group also had S/S and A/A genotypes.

The combination of genes and genotypes in the total number of patients repeated the above trend. It is noteworthy that the degree of occurrence of genotypes among genes is different, while ADRB2 (rs1042713) A>G gene genotypes A/A A/G were practically identical (47.5% and 52.5%, respectively), in ADRB3 (rs4994) Trp64Arg gene Trp /Trp genotype showed a clear superiority over the Trp/Arg genotype (94.6% 10.2%, respectively), PPARG2 (rs1801282)_C34G gene had a clear superiority in the S/S genotype compared to the S/G and G/G genotypes (52.5% vs. 39.0% and 5.1%). If we look at the indicators of the main and control groups, we note that the Trp/Trp genotype is more common in both groups - 94.9% (n=56) and 86.7% (n=13), respectively.

Although a gender difference was observed in encounter rates, no significant difference in encounter tendency was detected (Figure 1).

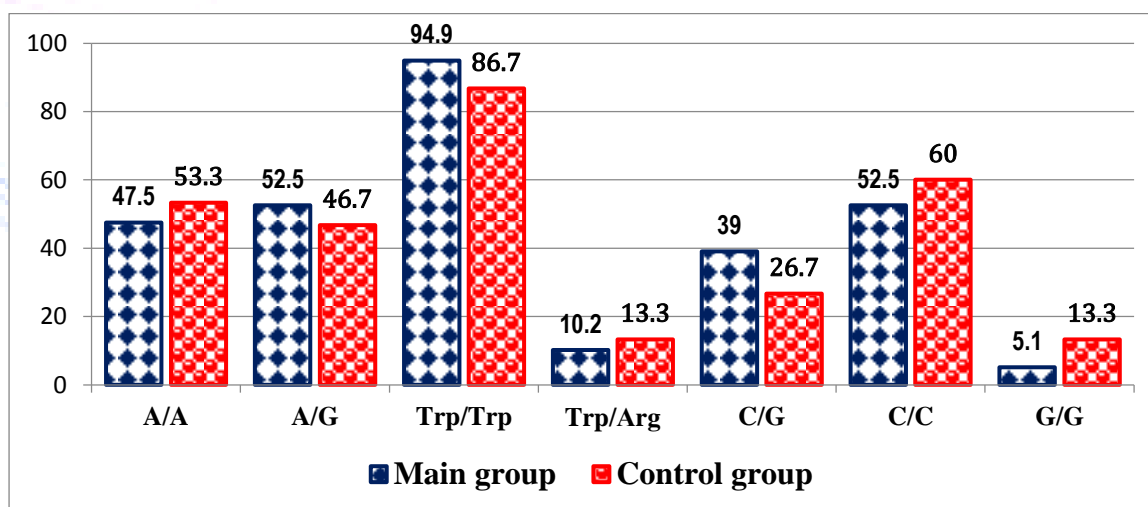


Figure 1. Percentage of comparative occurrence of genotypes in patients with diseases of the cardiovascular system

It can be seen that Trp/Trp, C/C, A/G, and A/A genotypes differed in both groups with higher frequency than other genotypes, with G/G being the least frequent genotype.

The obtained results showed that, in the main group, the studied genes and genotypes had different characteristics depending on the patients. Differences in patient height were not identified, indicating that there was no correlation between patients. It has been shown that these genes and genotypes are not associated with the height of patients diagnosed with CKD.

Similar indicators were obtained for TMI – Trp/Arg (average 31.0 units), G/G (average 30.0 units) and A/A (average 31.0 units) genotypes in the main group; in the control group, all indicators were practically the same, and genes directly related to TMI were not identified (Fig. 2).

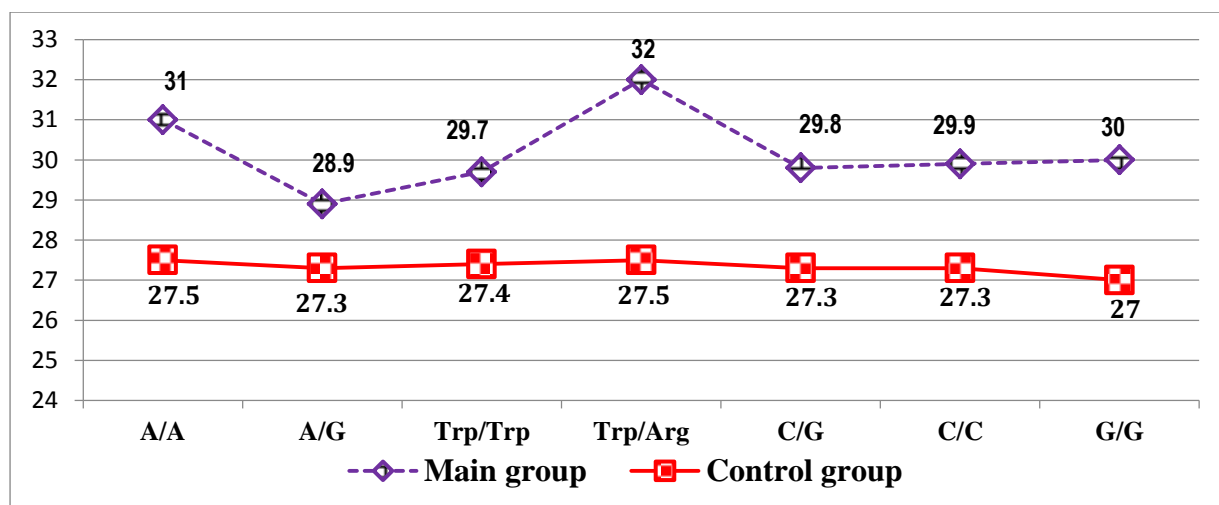


Figure 2. The degree of concordance of genes and genotypes with body mass index indicators in patients diagnosed with cardiovascular system, unit

Thus, the level of gene and genotypes of patients diagnosed with CKD is not related to their height, sharply different numbers corresponding to genotypes have not been determined. However, specificities related to the mass of patients were observed. The results showed that blood cholesterol levels in the control group were within the normal range (reference values from 3.1 $\mu\text{mol/L}$ to 5.0 $\mu\text{mol/L}$) in all cases. These values ranged from 3.9 $\mu\text{mol/L}$ to 4.5 $\mu\text{mol/L}$ on average, which proved to be within the reference range.

Table 2 Comparative indicators of the dependence of genes and genotypes on the level of cholesterol and fatty acids in the blood of patients with cardiovascular diseases

Genes	Genotypes	Cholesterol, (3,1-5 ммоль/л)		HDL (0,72-1,63 ммоль/л)		LDL (2,02-4,79 ммоль/л)	
		MG	CG	MG	CG	MG	CG
ADRB2(rs1042713) A>G	A/A	6.9 \pm 0,17*	4,3 \pm 0,16	2.93 \pm 0,3*	1,03 \pm 0,04	6.94 \pm 0,5*	2,54 \pm 0,19
	A/G	7.1 \pm 0,13*	4,1 \pm 0,13	2.95 \pm 0,2*	1,08 \pm 0,05	6.97 \pm 0,3*	2,31 \pm 0,13
ADRB3(rs4994) Trp64A _{rg}	T _{rp} /T _{rp}	7.2 \pm 0,0,12*	4,2 \pm 0,12	2.96 \pm 0,2*	1,05 \pm 0,04	6.95 \pm 0,3*	2,41 \pm 0,14
	T _{rp} /A _{rg}	7.4 \pm 0,3*	4,5 \pm 0,36	2.67 \pm 0,4*	1,04 \pm 0,04	7.04 \pm 0,2*	2,60 \pm 0,1
PPARG2(rs1801282)_C34 G	C/G	7.05 \pm 0,11*	3,9 \pm 0,18	2.89 \pm 0,3*	1,08 \pm 0,04	6.91 \pm 0,6*	3,0 \pm 0,13
	C/C	7.01 \pm 0,14*	4,3 \pm 0,16	2.97 \pm 0,2*	0,96 \pm 0,04	6.98 \pm 0,3*	2,29 \pm 0,14
	G/G	6.9 \pm 0,12*	4,4 \pm 0,26	3.01 \pm 0,3*	1,43 \pm 0,14	7.03 \pm 0,2*	3,35 \pm 0,6
Жами		7.05 \pm 0,12*	4,2 \pm 0,11	2,91 \pm 0,12*	1,10 \pm 0,03	6.97 \pm 0,2*	2,64 \pm 0,12

Note: MG is the main group, CG is the control group. *- a sign of reliability between the main and control groups.

The highest number of indicators of the control group corresponded to the Trp/Arg genotype of the ADRB3 (rs4994) Trp64Arg gene (4.5 $\mu\text{mol/L}$) and the G/G genotype of the PPARG2(rs1801282)_C34G gene (4.4 $\mu\text{mol/L}$). However, it should be noted that the obtained results are very close to each other in the control group, and clearly different parameters have not been identified. In the main group, the difference was evident ($P < 0.002$), all parameters of the obtained patients were significantly higher than the standard values (3.1-5.0 mmol/l) - on average 6.9 mmol/l to 7.4 $\mu\text{mol/L}$ up to /l. The most common detection of genes and genotypes was similar to the control group - the Trp/Arg genotype belonging to the ADRB3(rs4994) Trp64Arg gene - an average of 7.4 mmol/l.

A similar indicator was observed in A/G (average 7.1 mmol/l) and Trp/Trp genotype (average 7.0 mmol/l) ($P < 0.05$).

It was found that the presence of excess weight in patients (the main group) genotypes (Trp/Arg, G/G, A/A) that determined high BMI were also observed in the case of high cholesterol in the blood, the same genotypes increased body mass, high TMI, cholesterol in the blood it has been proven that it is related to the increased concentration. These conditions were the main reason for the origin of the CKD in patients, and such conditions were interpreted as the main characteristics of the distribution of gene-genotypes for patients with excess body weight.

Taking into account the high role of high and low density lipoproteins (YuZLP and PZLP) in overweight and obesity, their dependence on genes and genotypes of patients and control group was compared (Fig. 3).

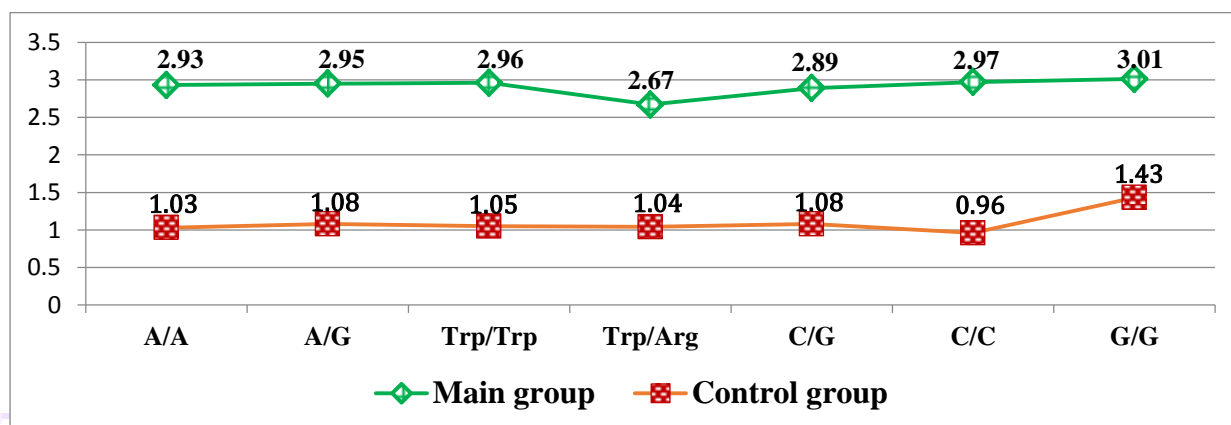


Figure 3. Comparative indicators of the amount of HDL in the blood of patients diagnosed with CKD depending on the genotypes, μmol/l

As can be seen from the indicators, the highest indicator in both groups was associated with the G/G genotype - 3.01 mmol/l and 1.43 mmol/l, respectively ($P < 0.05$). This situation was the same in both groups. However, in contrast, patients with Trp/Trp and S/S genotypes had higher values - on average 2.96 mmol/l and 2.97 mmol/l, respectively ($P < 0.05$). No such significant difference was observed in the control group.

In addition, the parameters of the control group were within the norm (reference values 0.72-1.63 mmol/l), the parameters of the main group were significantly higher than the norm data - on average 2.67 mmol/l to 3.01 mmol/l up to All indicators were inextricably linked with high body mass, TMI, cholesterol levels in the blood, but no such correlation was observed in the control group. Therefore, such dependencies in the main group were interpreted as "pathological dependencies", and dependencies in the control group were interpreted as "physiological dependencies".

CONCLUSION

Among the 7 genotypes of 3 genes in the polymorphism of genes and genotypes in cardiovascular diseases, the Trp/Trp genotype of the ADRB3 (rs4994)_Trp64Arg gene was the most frequent in the main and control groups, and the C/C genotype of the PPARG2(rs1801282)_C34G gene was moderately frequent in the main control group. ADRB2 (rs1042713) A/G gene A/A genotype was less common than Trp/Trp and C/C genotypes. The remaining PPARG2 (rs1801282)_C34G gene G/G genotype differed between the primary and control groups.

When studying the characteristics of genes and genotypes of cholesterol, HDL and LDL in the blood of patients diagnosed with CKD, it was found that all three indicators were significantly higher than

the standard parameters in the main group, while the data of the control group were within the standard parameters.

While the cholesterol, HDL and LDL content of the 7 genotypes of genes were high in the main group before hypocaloric diet therapy, after hypocaloric diet therapy, these indicators showed dramatic changes, while it was proved that these indicators did not change in the control groups.

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